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rejection. Applicants contend that the Examiner has not established a prima facie case of obviousness. It is well established that in order to establish a prima facie case of obviousness, one of the criteria that must be shown is a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine the reference teachings. The Examiner has not shown any suggestion or motivation to combine the references. The Examiner merely supports his conclusion of obviousness by saying that the "prior art in combination provided the motivation and a reasonable expectation of success." The Examiner has not provided any rationale or evidence for his conclusion. Accordingly, applicants contend that the Examiner has not established a prima facie case of obviousness. Applicants contend that these remarks obviate the above rejection and respectfully request that the Examiner reconsider and withdraw this ground of rejection.

INFORMATION DISCLOSURE STATEMENT

In accordance with the duty of disclosure under 37 C.F.R. §1.56, applicants would like to direct the Examiner's attention to the following references which are listed on PTO-1449 form attached hereto as **Exhibit B**. Copies of these references are attached hereto as **Exhibits 1-20**. A check which includes the \$180.00 fee for submission of an information disclosure statement pursuant to 37 C.F.R. §1.17(p) is enclosed.

1. Adluri, S., et al. (1995) "Immunogenicity of synthetic TF-KLH (keyhole limpet hemocyanin) and sTn-KLH conjugates in colorectal carcinoma patients." Cancer Immunol. Immunother.

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- 41: 185-192 (**Exhibit 1**);
2. Bernhard, H., et al. (1992) "Immunorecognition of ganglioside epitopes on human normal and melanoma tissues." Int. J. Cancer 51: 568-572 (**Exhibit 2**);
 3. Brezicka, F. T., et al. (1989) "Immunohistological detection of fucosyl-GM1 ganglioside in human lung cancer and normal tissues with monoclonal antibodies." Cancer Res. 49: 1300-1305 (**Exhibit 3**);
 4. Cheung, N-K. V., et al. "Monoclonal antibody to a glycolipid antigen on human neuroblastoma cells." Cancer Res. 45: 2642-2649 (**Exhibit 4**);
 5. Cheung, N-K. V., et al. (1987) "Ganglioside GD2 specific monoclonal antibody 3F8: a phase-I study in patients with neuroblastoma and malignant melanoma." J. Clin. Oncol. 5: 1430-1440 (**Exhibit 5**);
 6. Dippold, W. G., et al. (1985) "Immunohistochemical localization of ganglioside GD3 in human malignant melanoma, epithelial tumors, and normal tissues." Cancer Res. 45: 3699-3705 (**Exhibit 6**);
 7. Finn, O. J., (1995) "Immunotherapy: tumor vaccines." Proc. Am. Assoc. Cancer Res. 36: 675 (**Exhibit 7**);
 8. Hamilton, W. B., et al. (1993) "Ganglioside expression on

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human malignant melanoma assessed by quantitative immune thin-layer chromatography." Int. J. Cancer 53: 566-573 (Exhibit 8);

9. Helling, F., et al. (1994) "GD3 vaccines for melanoma: superior immunogenicity of keyhole limpet hemocyanin conjugate vaccines." Cancer Res. 54: 197-203 (Exhibit 9);
10. Helling, F. et al. (1995) "GM2-KLH conjugate vaccine: increased immunogenicity in melanoma patients after administration with immunological adjuvant QS-21." Cancer Res. 55: 2783-2788 (Exhibit 10);
11. Kensil, C. R., et al. (1991) "Separation and characterization of saponins with adjuvant activity from *Quillaja saponaria* molina cortex." J. Immunology 146: 431-437 (Exhibit 11);
12. Livingston, P. O., et al. (1994) "Improved survival in stage III melanoma patients with GM2 antibodies: a randomized trial of adjuvant vaccination with GM2 ganglioside." J. Clin. Oncol. 12: 1036-1044 (Exhibit 12);
13. Livingston, P.O., et al. (1994) "Phase I trial of immunological adjuvant QS-21 with a GM2 ganglioside-KLH conjugate vaccine in patients with malignant melanoma." Vaccine 12: 1275-1280 (Exhibit 13);
14. Livingston, P.O. (1995) "Approaches to augmenting the immunogenicity of melanoma gangliosides: from whole melanoma cells to ganglioside-KLH conjugate vaccines." Immunological

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Reviews 145: 147-166 (Exhibit 14);

15. Livingston, P.O., et al. (1989) "Characterization of IgG and IgM antibodies induced in melanoma patients by immunization with purified GM2 ganglioside." Cancer Res. 49: 7045-7050 (Exhibit 15);
16. Livingston, P.O., et al. (1997) "Tumor cell reactivity mediated by IgM antibodies in sera from melanoma patients vaccinated with GM2-KLH is increased by IgG antibodies." Ca. Immunol. And Immunotherapy 43: 324-330 (Exhibit 16);
17. Nilsson, O., et al. (1986) "Detection of a ganglioside antigen associated with small cell lung carcinomas using monoclonal antibodies directed against fucosyl-GM1." Cancer Res. 46: 1403-1407 (Exhibit 17);
18. Ragupathi, G. (1997) "Phase I trial with GD3-lactone-KLH conjugate and immunological adjuvant QS-21 vaccine with malignant melanoma." Proc. Am. Assoc. Cancer Res. 38: 398 (Exhibit 18);
19. Vangsted, A.J., et al. (1991) "Immunochemical detection of a small cell lung cancer-associated ganglioside (FucGM1) antigen in serum." Cancer Research 51: 2879-2884 (Exhibit 19); and
20. Zhang, S., et al. (1997) "Selection of tumor antigens as targets for immune attack using immunohistochemistry. I. Focus on gangliosides." Int. J. Cancer 73: 42-49 (Exhibit 20).

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Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. claims 1-2, 5-8 and 11-16.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone either of them at the number provided below.


No fee, other than the enclosed \$640.00 fee, which includes the \$460.00 fee for a three-month extension of time and the \$180.00 fee for submission of an information disclosure statement under 37 C.F.R. 1.17(p), is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.



1-22-02
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